JSC, Institute for Research develop new drug delivery system

In the future, microcapsules injected directly into human tissue may be the drug delivery system of choice to treat cancer and other diseases.

NASA and the Institute for Research, Inc., based in Houston, have jointly developed and co-patented a new drug delivery system that enables various drugs to be encapsulated for injection directly into tissue. This new technology, recently on display during Inspection 98, presents many opportunities for collaboration with pharmaceutical companies to develop new drug delivery systems for selected medical therapies, including chemotherapy.

The focus of the research by Dr. Dennis Morrison, principal researcher for JSC, and Dr. Benjamin Mosier, president of the Institute for Research, Inc., has been on making tiny microcapsules, slightly larger than white blood cells and similar to miniature water balloons, that can be injected into an artery leading into a large, solid tumor. Because they are too large to pass through the arterial bed, the microcapsules lodge there, creating an artificial clot or emboli that constricts the blood supply to the tumor. Diffusion causes the drug to leak through the outer skin of the capsule, creating a sustained release of anti-cancer drug directly inside the tumor. A tumor about one inch in diameter or larger may be treated effectively using this technique.

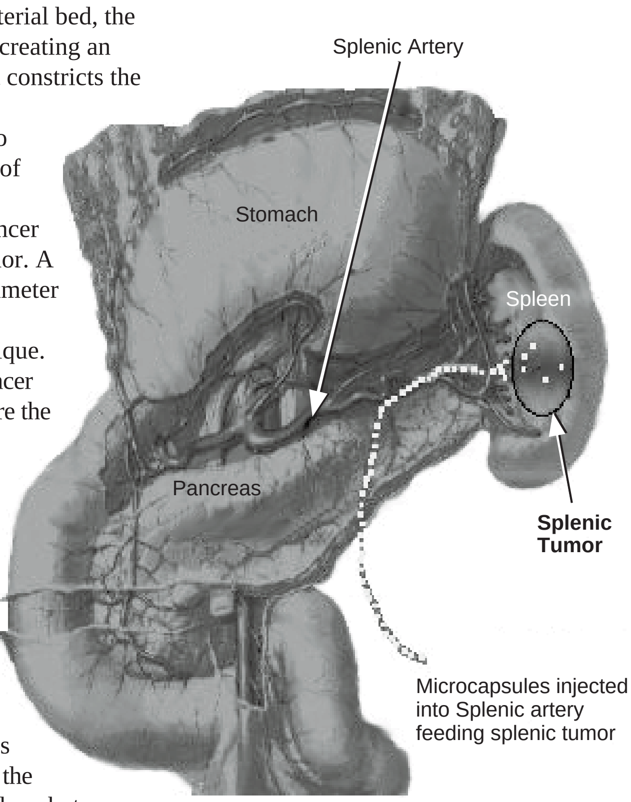
With this technology, cancer patients do not have to endure the debilitating side effects of having the anti-cancer drug circulating throughout their entire body. Moreover, because the tumor is treated directly, between one one-hundredth and one five-hundredth the normal systemic dose of medication is required. The surgeon does have to insert a catheter into the artery to carry out the procedure, but now very small catheters may be very carefully maneuvered into arteries to enter specific portions of major organs.

The microcapsules are made from liquids that differ significantly in density. As a result, the fluids tend to form two or three layers when blended together on Earth, with the densest material accumulating on the bottom and the least dense rising to the top.

For this reason, researchers have used the weightless environment of space to make these capsules. Microencapsulation experiments have been flown on nine shuttle flights including STS-95. Not only anti-cancer drugs but also a clot-dissolving enzyme, an antibiotic and an anti-nausea drug have been encapsulated in space.

JSC photo S98-20313 by Benny Benavides

Dr. Benjamin Mosier, president of the Institute for Research, Inc., left, and Dr. Dennis Morrison, principal researcher for the Johnson Space Center, examine an image of microcapsules produced during the STS-95 mission.



In space, surface tension becomes the predominant physical force, which makes liquids try to become spherical. The formulas for the liquids have been optimized so that they make spherical capsules. Then a polymer skin forms on the outside of each sphere as a thin membrane, thus making the miniature water balloon.

An additional step in the process allows the capsules to be detected in the body after injection. Adding as little as five to 10 percent of a radio-contrast oil inside the capsules allows physicians to locate them with a CT radio scan to confirm that they are in the tumor and not in healthy tissue.

If CT scans show that the microcapsules have somehow found their way into healthy tissue instead of into the tumor, another technique co-invented by Morrison and Mosier allows physicians to remove the microcapsules lodged in the arteries. In the presence of a magnetic field that does not harm the body, such as a magnetic resonance imaging scan, little ceramic-magnetic particles embedded inside of the capsules are designed to heat up to a temperature just slightly warmer than that of the outer skin around the capsules. The particles melt a tiny hole in the microcapsule, causing it to deflate and dump its contents. The contents and the empty microcapsules pass through the capillaries, and the anti-cancer drug is diluted as it enters the bloodstream.

This technique involving a "burst release" of encapsulated drugs using a magnetic field may have many applications, according to Morrison and Mosier.

"This technology opens up the possibility that for other kinds of drug delivery systems, we can have a burst release of drugs after the microcapsules have been injected, and we can control that procedure by magnetic fields normally used for diagnostic imaging," said Morrison.

As happens on the ground, the little magnetic particles, when mixed, tend to settle away from the interface between the liquids where the microcapsules are being formed. So research in microgravity is being used for many purposes: to show what kinds of microcapsules can be made, to improve the encapsulation process so that they can be made with not only one drug but with multiple drugs and with a radio contrast oil, and to determine how much of each element (the drug and the radio contrast oil) needs to be included to optimize effectiveness and to allow physicians to find out if the capsules are properly distributed throughout the target tissue. Lastly, microgravity is helping researchers study how to make more uniform capsules and how to make them in larger quantities on Earth.

"In space, control of the fluid processing is a lot easier," said Morrison. "Research done in space helps us determine the fluid flows and the chemical composition of the different liquids to help us develop the best microcapsules. It provides a tool to help us develop and scale up the technology to make the optimum microcapsules here on Earth."

The planned use of the new microcapsules is similar to another therapeutic method called Transcatheter Embolization (TCE), which also delivers the same drug and radio contrast oil directly into the tumor. In TCE, the mixture of drug and oil is injected into the artery leading to the tumor, followed by an injection of Gelfoam particles. These particles then swell to block the blood vessels in and around the tumor so that the treatment does not prematurely "wash out" of the tumor. Using this technique has improved the one-year survival rate of patients with inoperable liver tumors from 18 percent to between 55 and 69 percent.

"The advantage of the TCE technique is that it provides a way to keep the drug in the tumor longer," said Mosier. "The disadvantage is that it is difficult to control how much drug is washed through before the Gelfoam particles actually plug the arterial flow. We believe that we have a better way of doing the embolization with our microcapsules because they form the artificial emboli and they carry the drug inside."

NASA has patented this technology. The patent was issued on Oct. 27, the same day that the Microencapsulation Electrostatic Processing System, a new apparatus used to process encapsulated drugs, was loaded into the SPACEHAB for its first flight test. Payload Specialists John Glenn and Chiaki Mukai and Mission Specialist Pedro Duque operated the microencapsulation experiments during STS-95.

Mosier has exclusively licensed the technology back and is now attempting to forge alliances with drug companies to begin product development to take it to market. Three to five years will be needed to obtain approval from the Food and Drug Administration, depending upon requirements for clinical use of this new drug delivery system. ■